

Combine Effect of Injection Pressure and Diffuser at Exhaust Manifold for Single Cylinder CI Engine using Diesel and Palm Biodiesel

Kintesh D Patel^{1*}, Dr. Tushar M Patel², Gaurav P Rathod³

^{1*}M.E. Scholar, Mechanical Engineering Department, LDRP-ITR, Gandhinagar, India.

²Professor, Mechanical Engineering Department, LDRP-ITR, Gandhinagar, India.

³Lecturer, Mechanical Engineering Department, Govt. Polytechnic, Godhra, India.

Abstract: The combustion procedure in the internal combustion engine is varying cycle to cycle while varying load, speed, etc. It is difficult to accomplish better fuel economy and decrease pollution emissions. Literature shows that the design of a taper, straight and lower thermal inertia exhaust manifold takes good mass conservation, fuel economy and engine efficiency, Back pressure on engine having a powerful influence on engine efficiency and need to be decreased by using diffuser shape exhaust manifold. There is controlling parameter by which we can achieve good fuel economy and decrease exhaust gas pollution. Injection pressures in diesel engines play a significant role in engine performance and emissions obtaining Process of combustion. In this experimental study, effects of injection pressure and exhaust manifold on engine performance and exhaust emissions have been analysis. In experiment injection pressure take 200, 180 and 160. Experiments have been carried out on a single cylinder 4-stroke diesel engine by using Diesel and palm biodiesel.

Keywords: Engine performance, Exhaust emission, Biofuel, Injection pressure, Diffuser, Exhaust manifold.

I. Introduction

As recent year, numerous analysts have concentrated on the study alternative fuel, which advantage upgrading the engine monetary and emission characteristics. The primary pollutants from the conventional hydrocarbon fuel are unbound incompletely burned hydrocarbon (UBHC), CO, oxides of nitrogen (NO_x), smoke and particulate matter. It is the exceptional thermal efficiency of diesel engines unquestionably has preferences for preserving energy further more taking care of the greenhouse issue [2]. These reasons have forced us to find suitable alternate fuels. To improve the design of the exhaust system to fulfill the necessity of consumer is more engine power and eco-friendly. Along this line, satisfactory design of exhaust manifold geometry is required for improving gas exchange procedure. Exhaust manifolds are commonly made of simple cast iron or stainless steel which take the engine exhaust gas from the cylinder and deliver it to the exhaust pipe. Exhaust manifolds are too large will cause the exhaust gas to expand and slow down, minimizing the scavenging effect and that are too small will produce exhaust gas flow resistance which reducing power and dilute the incoming intake charge. Exhaust temperature of CI engine is lower due to their greater expansion ratio and are generally in the range of 200°C - 600°C. There are few factors that the engine designer changes provide low emission levels with high performance and good fuel economy. Few of these factors are the shape of the combustion chamber, the location and angle of the nozzle, the injection rate and nozzle spray pattern, injection timing, and camshaft timing. In present diesel engines, fuel injection systems are designed to obtain highest injection pressure [3]. So aim was to find the best performance parameter set by Taguchi method.

II. Literature Review

In the recent year, many research on the Engine Exhaust system. There are different exhaust manifold available like as nozzle, diffuser. J. Galindo et al. (2004) carried out experimental work on dual wall air gap exhaust manifold and conventional exhaust manifold. They concluded that dual wall air gap exhaust manifold improves transient performance of an engine due to saving exhaust energy by reducing heat loss to increase the catalyst temperature by 50 °C, increase in torque 6.6 % and volumetric efficiency [1]. Patil et al. (2014) Experimental work carried out at engine output condition is 5 kg load and 1500 rpm constant speed and found the result of fuel consumption rate is inversely proportional to the diffuser volume of exhaust manifold. Pressure at outlet of diffuser type exhaust manifold is directly proportional to the diffuser volume of exhaust manifold, which reduces the back pressure [5]. Patil et al. (2015) conclude that the increase in inlet cone angle increases the pressure of the flow which leads to reduce the recirculation zones. Installation of the EDS – II increases the brake thermal efficiency and decreases the backpressure [7]. Modi et al (2014) has been carried out for palm seed oil blended with diesel used in a single cylinder diesel engine. The results of the Taguchi experiment identify that 16 compression ratio, injection pressure 180 bar and engine load 10kg are optimum parameter

setting for highest brake thermal efficiency [6]. Patel et al. (2015) has been carried out Karanja biodiesel blended with diesel. As a result all the blends of Karanja biodiesel with diesel have considerable lesser Emission of HC, CO, CO₂, NOX as compared to diesel [8]. R.Rajappan et al. examined the performance, emission, and combustion qualities of a multi fuel variable compression ratio engine run with waste plastic oil and diesel blend as fuel and contrast and standard diesel. He presumed that the break thermal efficiency of the mix B30 is higher than standard diesel. The hydrocarbon emission of different mix is higher at higher pressure proportion [10]. Sanjeev et al. experiment were directed utilizing WPO, JME and Diesel mixes. He presumed that Break thermal efficiency reduces as blend ratio is increments after 20%. BSFC reduces with increments in load. Likewise infer that JME and WPO mixes are great option fuels for diesel engine [9].

III. Palm Bio-Diesel

Evaluation of the carbureting quality of vegetable oils requires the determination of their physical and chemical characteristic, such as: calorific value, Cetane level, distillation curve, viscosity, cloud point etc. Table 1 compares the physical-chemical properties of palm biodiesel to that of petroleum diesel. It is observed that the trans-esterification reaction reduces the calorific value of palm biodiesel, as well as its density, cloud point, sulphur content and carbon residue as compared petroleum diesel. Palm biodiesel has a lower calorific value, however, the higher Cetane level compensates for this disadvantage, i.e., palm biodiesel has higher quality combustion, making maximum use of its energy content. In addition, distillation of palm biodiesel show that the fuel is volatile with the dynamic viscosity, increasing with the palm oil content. However, the tendency of palm biodiesel to form carbon during combustion is observed to be less compared to petroleum diesel.

Table 1: The fuel Properties of Palm seed oil and Diesel

Property	Palm biodiesel	Diesel
Kinematic viscosity at 40°C (cSt)	4.8	3.0
Density@ 15°C kg/m ³	876	833
Flash point(°c)	130°C	74°C
Fire point(°c)	171°C	120°C
Cetane number	62.8	49
Calorific value(kJ/kg)	38600	42850
Pour point(°c)	17°C	-25°C

IV. Exhaust Manifold

The environment which a contending exhaust system, and specially engine head, must survive. It can only be described as a brutal combination of temperatures, stresses, corrosion and vibration. The exhaust technology can help decrease the problems and help to increase the potential gains of the system. There are two separate components to the exhaust event. The first is the removal of exhaust gasses from the cylinder, which occurs as a pulse of hot gas exiting the cylinder and flowing down the header primary tube. The second is the (much faster) travel of the pressure wave in the port caused by the pressure spike which occurs when the exhaust valve opens, and the various reflections of that wave [4]. Taking suitable advantage of these pressure waves (component two) can create dramatic improvements in clearing the cylinder (component one) and can powerfully assist the inflow of fresh charge [11]. In automotive engineering, an exhaust manifold gain the exhaust gases from multiple cylinders into one pipe. Exhaust manifolds are normally made from cast iron or stainless steel units which gain engine exhaust gas from multiple cylinders and deliver it to the exhaust pipe. The high pressure head is produce by the high pressure difference between the exhaust in the combustion chamber and the atmospheric pressure outside of the exhaust system [12]. The instantaneous pressure evolution imposed by the manifold at the exhaust valve dependent essentially on the layout and dimensions of the pipes, so that an adequate design of the manifold geometry can improve the engine power, efficiency, and decrease the emissions of pollutants.

Figure 1 Shows Diffuser A, It was made from cast iron. It has outer diameter (61.50mm), inner diameter (31.50mm), length (58mm), and angle with center axis (14.5°).

Figure 2 Shows Diffuser B, It was made from aluminum. It has outer diameter (60.50mm), inner diameter (33.50mm), length (79.50mm), and angle with center axis (10°).

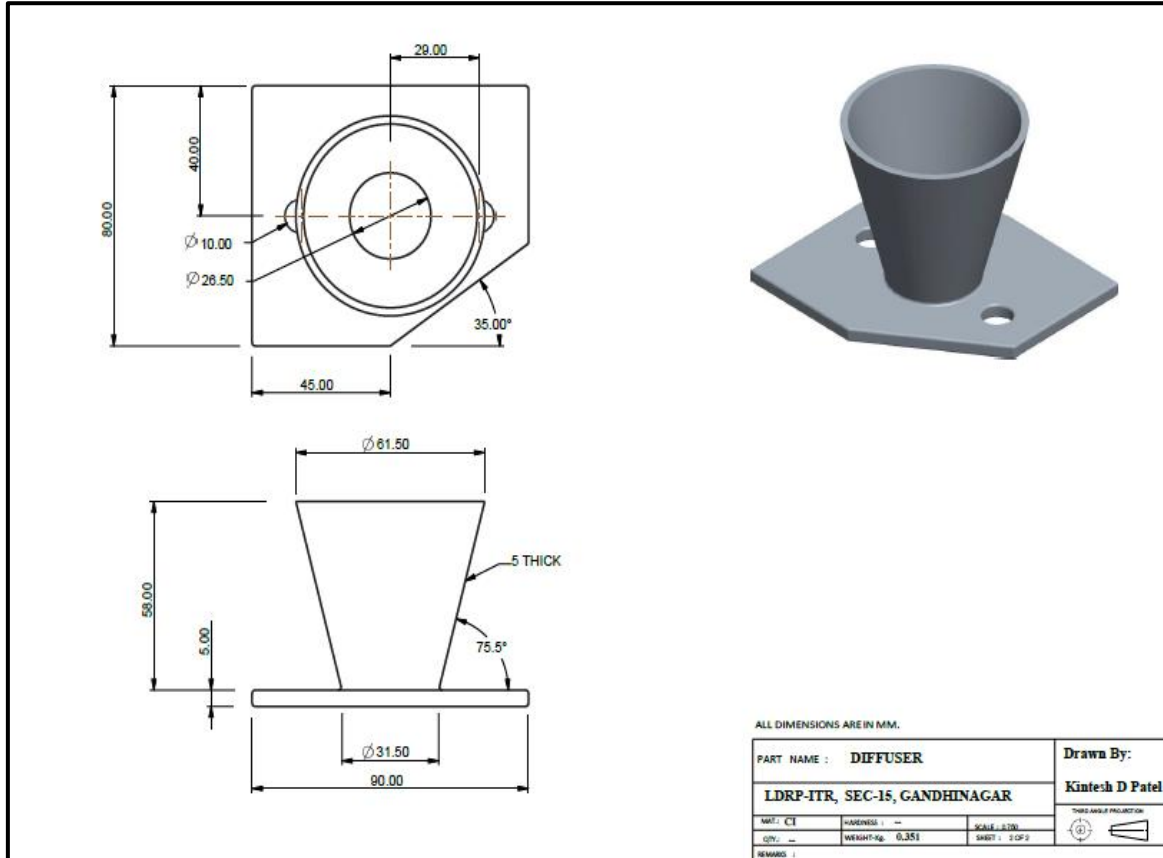


Fig 1: 2D-3D Drawing of Diffuser A

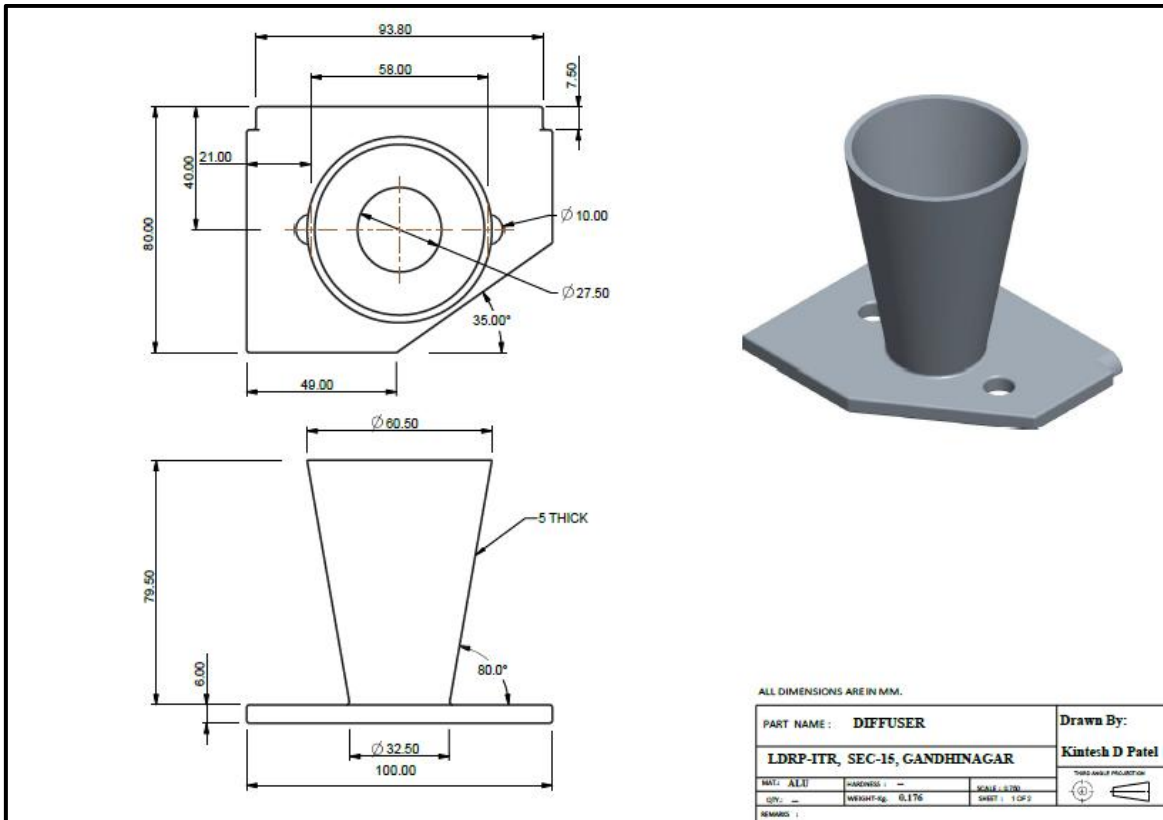


Fig 2: 2D-3D Drawing of Diffuser B

V. Experiment Set Up

In this experiment, single cylinder IC Engine is used and attached with the eddy current dynamometer with the help of flywheel shaft, varies the load on the engine or load remain constant. Exhaust Gas analyzer is used to find the emission characteristic of exhaust gas from engine. The reading takes by varying the load on the engine using the dynamometer. The mode of operation in this engine can be changed from diesel to Petrol or from Petrol to Diesel with some needed changes. In both operation modes the compression ratio can be changed without stopping the engine and no other changes needed for the geometry of combustion chamber by specially designed tilting cylinder block arrangement. Different other instruments are provided to interface are airflow, fuel flow, temperatures and load measurement devices. For cooling water and calorimeter water flow measurement Rota meter is provided. For auto start of engine a battery, starter and battery charger is provided. Analysis software Engine-soft is provided for on line performance evaluation and lab view based Engine Performance. The test engine used in this experiment is as shown in figure 3.

Different engine performance parameters such as Brake power, indicated power, specific fuel consumption etc. and emission contents such as CO, CO₂, NO_x and HC found from the experiments. In this experiment first engine performance and emission is measured by only using diesel as a fuel. After that the engine performance and emission is measured by diesel with diffuser type exhaust manifold. Then same reading taking with palm biofuel. Compare the results coming out for different exhaust manifold with the only used diesel as a fuel. Than the analysis is being made for which exhaust manifold and biofuel have a best optimized performance and emission characteristics for particularly used diesel engine compared to diesel fuel. Engine Specification as shows in table 2.

Table 2: Engine setup specifications[IC Engine Manual]

Engine manufacturer	Apex Innovations (Research Engine test set up)
Software	Engine soft Engine performance analysis software
Engine type	Single cylinder four stroke multi fuel research engine
No. of cylinder	1
Type of cooling	Water cooled
Rated Power	3.5 kW @ 1500 rpm
Cylinder diameter	87.5 mm
Orifice diameter	20 mm
Stroke length	110 mm
Connecting rod length	234 mm
Dynamometer	Type: eddy current, water cooled, with loading unit

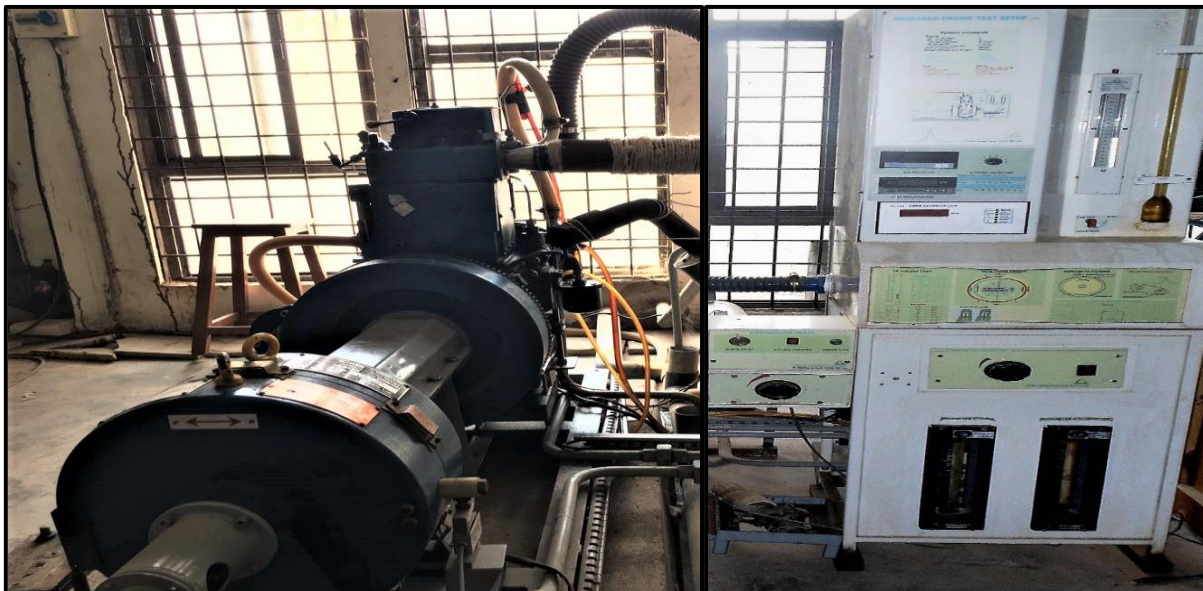


Fig. 3: Engine setup with diffuser.

VI. Observation Table And Result Table

The observed data find out by experiment on diesel engine by using pure diesel and palm biodiesel as a working fuel for various Injection pressure is given in table 3.

Table 3: Observation Table for Various Injection Pressure

For Diesel fuel, Density: 833 kg/m ³ , Calorific value : 42850 kJ/kg Parameter : Injection Pressure, Load						For Palm Biodiesel fuel, Density: 876 kg/m ³ , Calorific value : 38600 kJ/kg Parameter : Injection Pressure, Load					
Ex. No	Diffuser	IP	Load (kg)	RPM	FC (cc/min)	Air (mmwc)	O ₂ (%)	CO ₂ (%)	HC (ppm)	CO (%)	NO _x (ppm)
1	No	200	1.05	1541	8	59.94	19.15	0.9	34	0.06	87
2	No	180	7.07	1505	14	56.88	18.04	1.6	35	0.03	445
3	No	160	13.04	1465	19	52.8	16.97	2.1	38	0.02	1096
4	diffuser-A	200	7.21	10497	15	57.55	15.12	4.2	39	0.05	887
5	diffuser-A	180	12.64	1465	19	54.46	15	4.2	60	0.08	1123
6	diffuser-A	160	0.9	1527	7	61.69	17.25	1.9	45	0.19	26
7	diffuser-B	200	11.63	1439	19	51.66	11.8	5.4	43	0.09	2400
8	diffuser-B	180	1.09	1496	7	60.33	17.63	1.8	46	0.13	265
9	diffuser-B	160	7.07	1489	13	59.27	19.2	0.922	39	0.063	68
10	No	200	1.05	1512	8	56.93	19.1	0.9	23	0.07	75
11	No	180	7.08	1504	14	56.73	18.03	1.6	27	0.03	399
12	No	160	13.1	1489	22	53.7	17.18	2.1	31	0.03	954
13	diffuser-A	200	7.16	1475	13	57.04	14.9	3.6	37	0.07	731
14	diffuser-A	180	13.2	1504	19	58.76	11.86	6	59	0.05	2330
15	diffuser-A	160	1.06	1518	6	61.09	17.61	1.08	61	0.1	342
16	diffuser-B	200	12.98	1502	23	53.44	11.27	6.3	50	0.11	2253
17	diffuser-B	180	1.06	1542	10	63.45	17.41	2	27	0.18	128
18	diffuser-B	160	7	1489	15	57.56	14.57	4.1	43	0.09	974

The result data obtained from the observed data for pure diesel and palm biodiesel fuelled in diesel engine for various Injection Pressure is given in table 4.

Table 4: Result Table for Various Injection Pressure

Ex. No.	Load (kg)	Torque (Nm)	IP (kW)	BP (kW)	FP (kW)	ITHE (%)	BTHE (%)	Mech. eff. (%)	Vol. eff. (%)	SFC (kg/kWh)	FC kg/hr.	Air kg/hr.
1	1.05	1.91	3.77	0.31	3.46	79.16	6.49	8.19	70.24	1.3	0.4	25.21
2	7.07	12.83	5.55	2.02	3.53	66.63	24.29	36.45	70.06	0.35	0.7	24.56
3	13.04	23.67	7.91	3.63	4.28	69.98	32.13	45.92	69.34	0.26	0.95	23.66
4	7.21	13.09	5.9	2.05	3.85	77.72	6.1	34.76	70.84	0.3	0.65	24.7
5	12.64	22.94	6.8	3.52	3.28	60.15	31.13	51.75	70.42	0.27	0.95	24.03
6	0.9	1.63	3.42	0.26	3.16	82.21	6.27	7.63	71.91	1.34	0.35	25.58
7	11.63	21.12	6.16	3.18	2.98	54.5	28.15	51.65	69.83	0.3	0.95	23.41
8	1.09	1.97	3.56	0.31	3.25	85.47	7.42	8.68	72.58	1.13	0.35	25.29
9	7.07	12.83	5.44	2	3.44	70.33	25.88	36.79	72.29	0.32	0.65	25.07
10	1.05	1.9	3.71	0.3	3.41	82.36	6.67	8.1	69.76	1.4	0.42	24.57
11	7.08	12.85	5.72	2.02	3.7	72.56	25.66	35.36	70.02	0.36	0.74	24.53
12	13.1	23.78	7.34	3.71	3.63	59.22	29.9	50.5	68.8	0.31	1.16	23.86
13	7.16	13	5.17	2.01	3.16	70.49	27.41	38.89	71.58	0.34	0.68	24.6
14	13.2	23.95	7.62	3.77	3.85	71.18	35.22	49.48	71.25	0.26	1	24.96
15	1.06	1.92	3.6	0.3	3.3	106.5	9.02	8.46	71.98	1.03	0.32	25.45
16	12.98	23.57	7.26	3.71	3.55	56.62	28.06	51.05	68.04	0.33	1.21	23.81
17	1.06	1.92	4.71	0.31	4.4	83.53	5.51	6.59	72.22	1.69	0.53	25.94
18	7	12.7	6.14	1.98	4.16	72.62	23.43	32.26	71.23	0.4	0.79	24.71

VII. Result And Discussion

In the experiment, Four parameters is consider like as fuel (Diesel and Palm Biodiesel), Diffuser (No, Diffuser A, Diffuser B), Injection pressure (200, 180, 160), Load (1, 7, 13). From this parameter to Discuss Brake thermal efficiency, specific fuel consumption and NO_x emission. This result discuss from the Minitab software Then Validation of Optimum set of Parameter.

7.1 Taguchi Analysis for Brake Thermal Efficiency

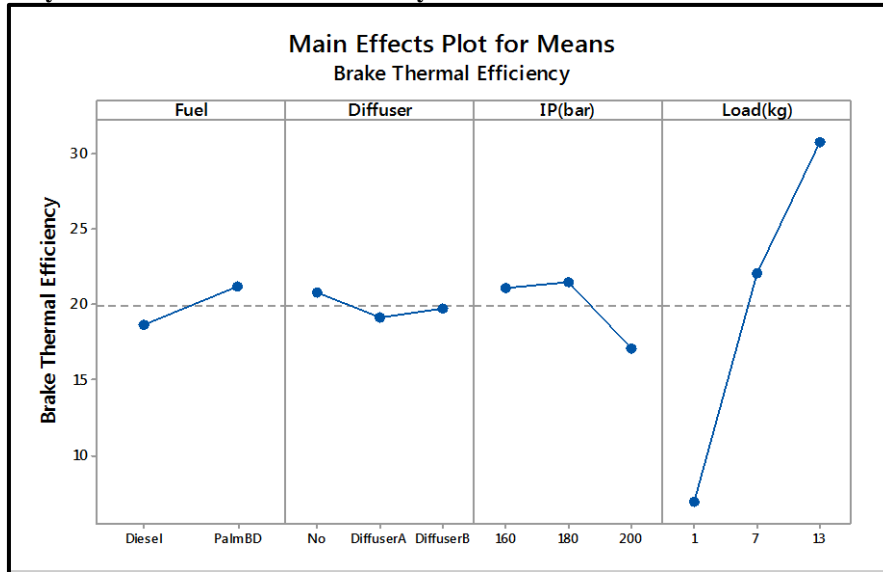


Fig. 4: Main Effects Plot for Means of Brake Thermal Efficiency

Table 5: Response Table for S/N Ratios of Brake Thermal Efficiency

Level	Fuel	Diffuser	CR	Load
1	23.36	24.71	25.06	16.67
2	24.91	23.39	24.82	26.00
3	-	24.31	22.52	29.73
Delta	1.54	1.33	2.54	13.07
Rank	3	4	2	1

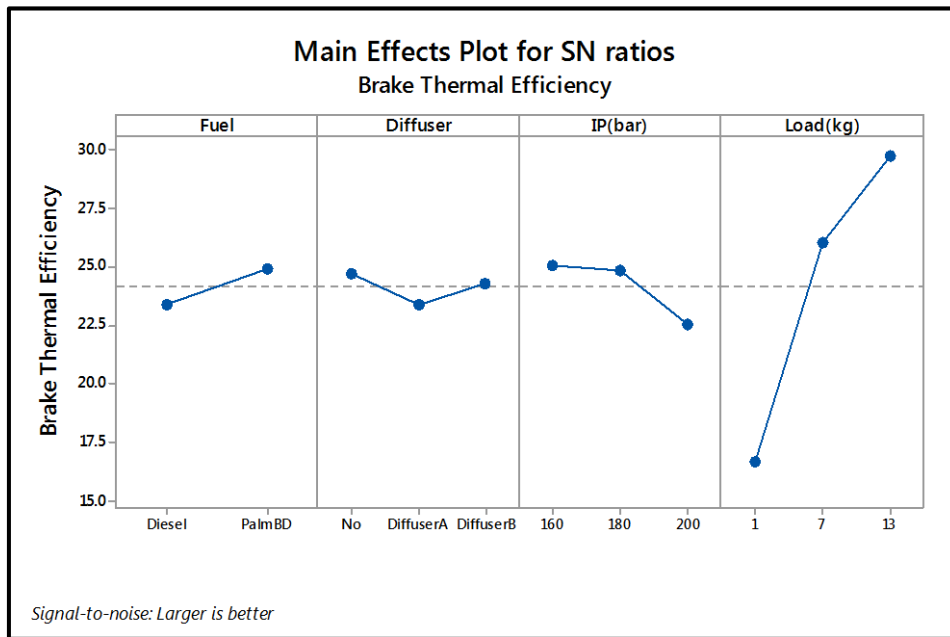


Fig. 5: Main Effects Plot for S/N ratios of Brake Thermal Efficiency

Response curve analysis is aimed at determining influential parameter and their optimum set of control parameters. Figure shows response at each factor level. The S/N Ratio for the different performance responses were is calculated at each factor.

The S/N Ratio for different performance response were calculated at each factor level and the average effect were determined by taking the total of each factor level and divided by the number of data points in the total. The greater difference between S/N ratio values the levels, the parametric influence will be much. The parameter level having the highest S/N ratio corresponds to the sets of parameters indicates highest performance.

The term optimum setting is reflects only optimal combination of the parameters defined by this experiment. The optimum setting is determined by choosing the level with the highest S/N ratio. Referring (figure.5) the response curve for S/N ratio, the highest S/N ratio was observed at Palm Biodiesel Fuel, Engine Load (13 kg), No Diffuser and Injection pressure (160 bar), which are optimum parameter setting for highest Brake thermal efficiency. From delta values as mention table 5, maximum (13.07) for engine load and minimum (1.33) for diffuser. Parameter engine load is most significant parameter and diffuser is least significant for Brake Thermal efficiency. Optimum parameter set as shown in table 6.

Table 6: Optimize Set of Parameter for Brake Thermal Efficiency

Fuel	Diffuser	IP	Load	BTHE (%)	SN Ratio
PalmBD	No Diffuser	160	13	34.15	32.00

Experiment has been carried out using optimum set of parameter. Experimental brake thermal efficiency for optimum set of parameter is 32.80 %. This experimental value is nearer to predicted value 34.15 % as shown in table 7.

Table 7: Validation Results for Brake Thermal Efficiency

Predicted Value	Experimental Value	% Variation
34.15%	32.20%	6.05

7.2 Taguchi Analysis for Specific Fuel Consumption

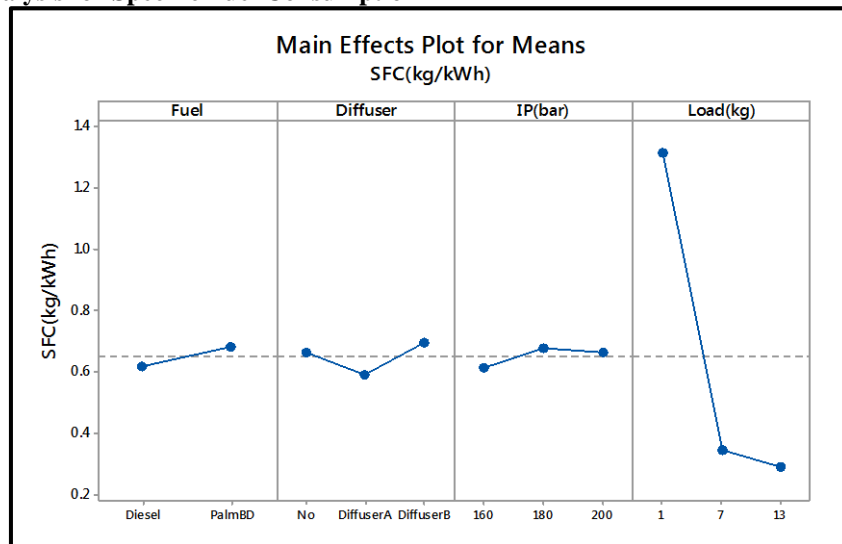


Fig. 6: Main Effects Plot for Means Specific Fuel Consumption

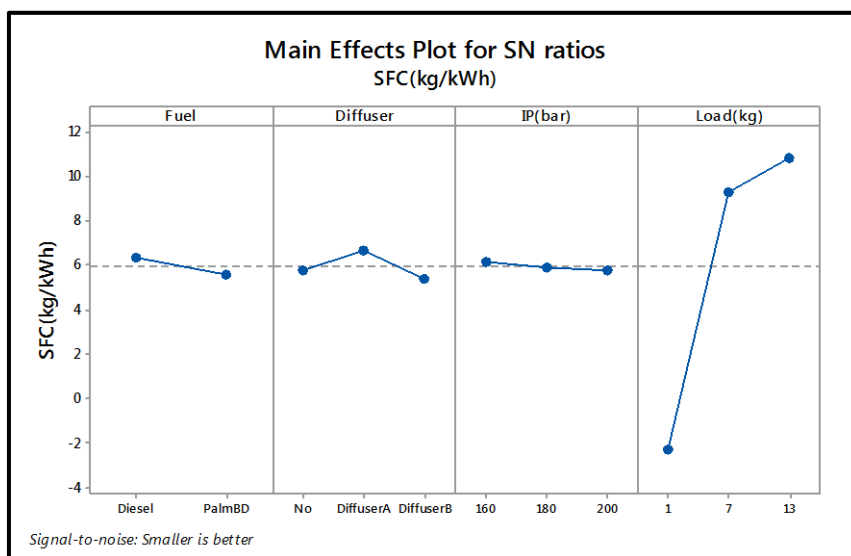


Fig.7: Main Effects Plot for S/N ratios of Specific Fuel Consumption

Table 8: Response Table for S/N Ratios of Specific Fuel Consumption

Level	Fuel	Diffuser	IP	Load
1	6.347	5.777	6.155	-2.270
2	5.552	6.684	5.908	9.279
3	-	5.387	5.786	10.839
Delta	0.795	1.296	0.369	13.109
Rank	3	2	4	1

The term optimum setting is reflects only optimal combination of the parameters defined by this experiment. The optimum setting is determined by choosing the level with the largest S/N ratio. Referring (figure 7) the response curve for S/N ratio, the largest S/N ratio was observed at Diesel fuel, Engine Load (13 kg), Diffuser A and Injection pressure (160 bar), which are optimum parameter setting for Smaller Specific fuel Consumption. From delta values as mention table 8, maximum (13.109) for engine load and minimum (0.369) for Injection pressure. Parameter engine load is most significant parameter and Injection pressure is least significant for Specific fuel Consumption. Optimum parameter set as shown in table 9.

Table 9: Optimize Set of Parameter for Specific fuel Consumption

Fuel	Diffuser	IP	Load	SFC (kg/kWh)	SN Ratio
Diesel	Diffuser A	160	13	0.158	12.17

Experiment has been carried out using optimum set of parameter. Experimental Specific fuel consumption for optimum set of parameter is 0.165 kg/kWh. This experimental value is nearer to predicted value 0.158 kg/kWh as shown in table 10.

Table 10: Validation Results for Specific fuel Consumption

Predicted Value	Experimental Value	% Variation
0.158 kg/kWh	0.165 kg/kWh	4.2

7.3 Taguchi Analysis for NO_x Emission

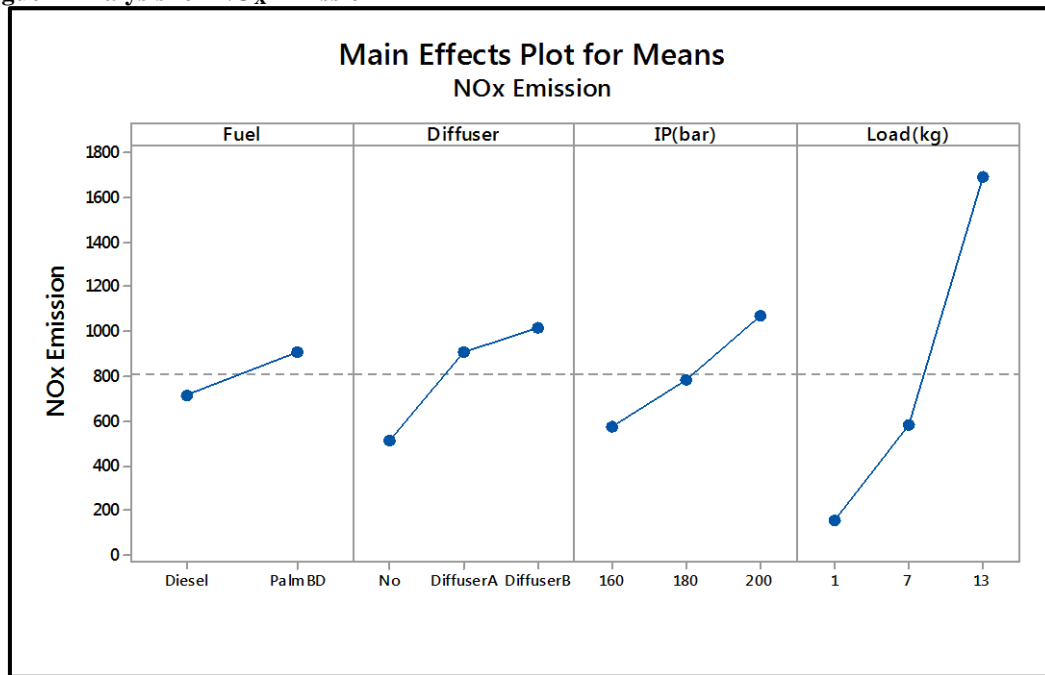


Fig. 8: Main Effects Plot for Means of NO_x Emission

Table 11: Response Table for S/N Ratios of NO_x Emission

Level	Fuel	Diffuser	IP	Load
1	-50.39	-50.28	-49.30	-40.98
2	-54.82	-53.93	-53.99	-52.94
3	-	-53.61	-54.53	-63.90
Delta	4.43	3.65	5.23	22.92
Rank	3	4	2	1

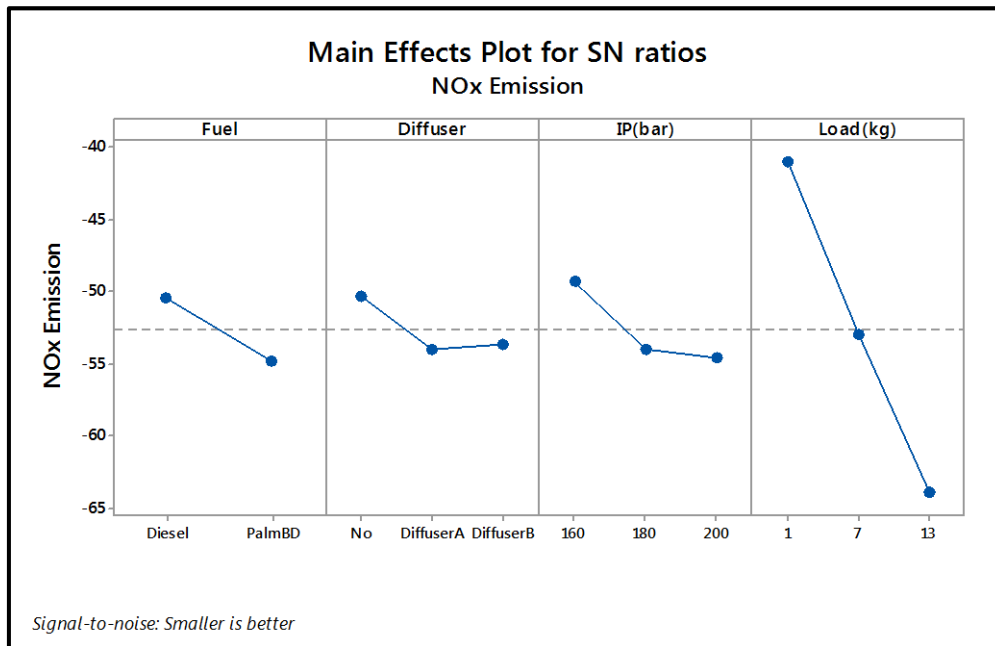


Fig. 9: Main Effects Plot for S/N ratios of NO_x Emission

The term optimum setting is reflects only optimal combination of the parameters defined by this experiment. The optimum setting is determined by choosing the level with the largest S/N ratio. Referring (figure 9) the response curve for S/N ratio, the largest S/N ratio was observed at Diesel Fuel, Engine Load (1 kg), No Diffuser and Injection pressure (160 bar), which optimum parameter are setting for Smaller NO_x Emission. From delta values as mention table 11, maximum (22.92) for engine load and minimum (3.65) for Diffuser. Parameter engine load is most significant parameter and Diffuser is least significant for NO_x Emission. Optimum parameter set as shown in table 12.

Table 12: Optimize Set of Parameter for NO_x Emission

Fuel	Diffuser	IP	Load	NO _x Emission (ppm)	SN Ratio
Diesel	No Diffuser	160	1	479.88	33.12

Experiment has been carried out using optimum set of parameter. Experimental NO_x Emission for optimum set of parameter is 450 ppm. This experimental value is nearer to predicted value 479.88 ppm as shown in table 13.

Table 13: Validation Results for NO_x Emission

Predicted Value	Experimental Value	% Variation
479.88 ppm	450 ppm	6.6

VIII. Conclusion

The Taguchi method was found to be an efficient technique for quantifying the effect of control parameters. Result discuss below:

- For Brake Thermal efficiency, Palm Biodiesel Fuel, No Diffuser, Injection pressure (160 bar) and Engine Load (13 kg), which are optimum parameter. This experimental value 32.80 % is nearer to predicted value 34.15 %.
- For Specific fuel Consumption, Diesel fuel, Diffuser A, Injection pressure (160 bar) and Engine Load (13 kg), which are optimum parameter. This experimental value 0.165 kg/kWh which nearer to predicted value 0.158 kg/kWh.
- For NO_x Emission, Diesel Fuel, No Diffuser, Injection pressure (160 bar) and Engine Load (1 kg), which are optimum parameter. This experimental value 450 ppm which nearer to predicted value 479.88 ppm.

References

- [1] J. Galindo , J. M. Lujan , J. R. Serrano , V. Dolz , S. Guilain, “Design of an exhaust manifold to improve transient performance of a high-speed turbocharged diesel engine” Experimental Thermal and Fluid Science 28 (2004) 863–875.
- [2] Patel, K. B., Patel, T. M., & Patel, S. C. (2013). Parametric Optimization of Single Cylinder Diesel Engine for Pyrolysis Oil and Diesel Blend for Specific Fuel Consumption Using Taguchi Method, 6(1), 83–88.
- [3] T. E, Faculty. (2013). An experimental investigation of the effect of the injection pressure on engine performance and exhaust emission in indirect injection diesel engines, 23, 2051–2060. [https://doi.org/10.1016/S1359-4311\(03\)00171-6](https://doi.org/10.1016/S1359-4311(03)00171-6)

- [4] Exhaust System Technology: Science and Implementation of High Performance Exhaust Systems.
- [5] Patil, A. A., Navale, L. G., & Patil, V. S. (2014). Experimental Investigation and Analysis of Single Cylinder Four Stroke CI Engine Exhaust System, 3(1), 1–6.
- [6] Modi, M. A., Patel, T. M., & Rathod, G. P. (2014). Parametric Optimization Of Single Cylinder Diesel Engine For Palm Seed Oil & Diesel Blend For Brake Thermal Efficiency Using Taguchi Method, 4(5), 49–54.
- [7] Patil, D. D., Kumbhare, S., & Thakur, K. K. (2015). CFD Analysis of Exhaust System and Effect of Back Pressure on Engine Performance, 1(1), 1–9.
- [8] Patel, M. A., Patel, P. R., Patel, T. M., & Rathod, G. P. (2015). Performance Analysis of Four Stroke Single Cylinder C I Engine Using Karanja Biodiesel-Diesel Blends. IOSR, Journal of Mechanical and Civil Engineering (IOSR-JMCE), 13(2).
- [9] Publications, K. S. (2015). Experimental Investigation on Performance of Direct Injection Diesel Engine Fuelled with Jatropa Methyl Ester, Waste Plastic Oil and Diesel Oil, 2(6), 72–75
- [10] Rajappan, R., Suresh, V., Udhayakumar, K., & Anbuselvan, D. (2015). Performance and emission characteristic of a variable compression ratio direct injection diesel engine using plastics oil. Journal of Chemical and Pharmaceutical Sciences, 7(7), 40–43.
- [11] Dole, N. B., & Bhangale, J. H. (2016). A review on effect of backpressure on exhaust system, 3(1), 163–168.
- [12] Rao, P., Abdulrahman, G. A., & Mahmood, S. (2016). Parametric Optimization through Numerical Simulation of VCR Diesel Engine. Journal of The Institution of Engineers (India): Series C, (x). <https://doi.org/10.1007/s40032-016-0298-x>